Movement Disorders
CLINICAL PRACTICE
REVIEW

Nocturia in Parkinson's Disease: Why Does It Occur and How to Manage?

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Abstract: **Background:** Nocturia is one of the commonest nonmotor symptoms in Parkinson's disease (PD) and has a significant impact on quality of life both for patients and their carers. There exists a relation between nocturia and poor sleep quality, falls, and institutionalization. Nocturia may manifest as a result of reduced functional bladder capacity or nocturnal polyuria; however, most often the cause is multifactorial. Disorders of circadian rhythm regulation are known to occur with sleep disturbances in PD may also contribute to nocturia.
Methods and Results: In this review, an overview of the assessment and management of nocturia in patients with PD is presented. History taking, medication review, and a bladder diary form the cornerstone of the evaluation. Urinalysis, ultrasonography, and urodynamic studies help to assess the cause for lower urinary tract symptoms and exclude concomitant pathologies, such as bladder outlet obstruction. Antimuscarinic medications are the first-line treatment for the overactive bladder; however, caution is needed when using these medications in individuals predisposed to cognitive impairment. Desmopressin is effective for managing nocturnal polyuria.
Conclusions: An individualized approach is recommended to optimize the management of nocturia in PD.

Parkinson's disease (PD) is characterized predominantly by motor complaints, consisting of bradykinesia, rigidity, and rest tremor and gait disturbances. However nonmotor symptoms (NMS) commonly accompany these motor symptoms.[1] Lower urinary tract (LUT) symptoms are common in PD and include *storage symptoms* (urinary urgency, increased daytime frequency, and nocturia, with or without incontinence) and *voiding symptoms* (urinary hesitancy, interrupted or poor stream, and double voiding).[2,3] The prevalence of LUT symptoms varies between 38% and 71%,[4,5] and its severity increases with progression of PD, paralleling other manifestations of autonomic dysfunction.[6] Urinary symptoms are an important cause for morbidity in PD, having a devastating impact on quality of life, and have been recognized by Parkinson's UK as one of the top 10 priority areas for research in PD.[7]

Using a standardized validated questionnaire of NMS, the NMS Quest, nocturia was found to be the most common LUT symptom, reported by more than 60% of participants.[8] Nocturia was, in fact, reported to be the commonest NMS reported in this study.

The cause for nocturia in PD is poorly understood; however, it is likely to be multifactorial.[9–11] We review the pathophysiology of nocturia in PD and principles for management.

Prevalence of Nocturia in PD

Questionnaire based studies generally report a high prevalence of nocturia, with figures ranging between 76%[12] and 86%,[13,14] though one study reported a prevalence of only 34.6%.[15] In a study of 115 PD patients using a questionnaire on pelvic organ functions, Sakakibara et al. reported nocturia (or nighttime frequency) in 53% of men and 63% of women with PD.[16]

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Nocturia has been reported in 34.6% of PD patients using a semistructured interview in 1,072 consecutive patients with PD in the large, multicentric PRIAMO study.[15]

This apparent variability in prevalence between studies could be put down to several factors, including differences in the demographic features of the cohort of patients being studied, and the occurrence of medical comorbidities. LUT symptoms are more prevalent with advancing disease and were most frequent in patients at H & Y stage 4 to 5 with a reported prevalence of around 90%.[15] Moreover, the term nocturia has been applied differently in studies and the prevalence varies according to the definition being used. The International Continence Society (ICS) made an attempt to standardize the definition of nocturia in 2002 and, based on a consensual approach, put forward "the complaint that the individual has to wake at night one or more times to void."[17]

The prevalence of nocturia is clearly greater in PD compared to the general population. In a questionnaire-based cross-sectional study using the American Urological Association-7 questionnaire,[18] LUT symptoms were reported in 39.3% of PD patients compared to 10.8% in an age-matched healthy control group.[19] Nocturia was reported by 63.9% of patients with LUT symptoms.[19]

The Impact of Nocturia

Most studies have demonstrated that nocturia has a significant negative impact on quality of life.[20,21] Awakening once at night is considered to be "normal" by many, and the degree of bother associated with nocturia increases with the frequency of nocturia. A recent population-based study demonstrated that having two voids or more per night was associated with impaired health-related quality of life (QoL).[22] A number of community-based studies have demonstrated that a high proportion of patients with nocturia perceive this to be a troublesome complaint.[23] In a large study, urinary incontinence was found to be major predictors of QoL in patients with PD using the 39-item Parkinson's Disease Questionnaire[24]; however, the question regarding nocturia was not specifically evaluated in this study.

Few studies have evaluated the bother associated with nocturia in patients with PD, and nocturia was reported to be bothersome in 50% in one questionnaire-based study.[14] QoL has been shown to be poor in PD patients reporting nocturia.[25] In general, LUT symptoms have an immense impact on QoL measures, early institutionalization, and health-related costs.[26] There exists an association between nocturia and the risk for falls[27] and hip fractures.[28] This becomes particularly relevant to PD where patients are at risk for falls, and a prevalence of 54% in PD patients compared to 18% in age-matched healthy participants was reported in one study.[29]

In a study of 63 PD patients using polysomnography, Vaughan et al. reported lower whole-night total sleep time and lower sleep efficiency.[30] Nocturia is an important cause for sleep fragmentation and poor sleep.[30] Additionally, the impact that PD-related symptoms has on carers and partners of patients is increasingly becoming recognized. Three quarters of carers who responded to a survey in the UK were needing help with day-to-day caring and of concern; however, fewer than one fifth were getting the support they required.[31] The carer burden attributed to frequent nighttime awakenings by a partner with PD and nocturia is yet to be studied systematically.

Causes for Nocturia

There are several causes for nocturia (Table 1). The commonest causes are reduced functional bladder capacity and nocturnal polyuria; however, these are not mutually exclusive and often occur concurrently in the same patient, known as mixed nocturia.[32]

Reduced Functional Bladder Capacity at Night

Functional bladder capacity is diminished if the bladder wall compliance is reduced, the detrusor is involuntarily contracting (detrusor overactivity or DO), or if the bladder has incompletely emptied following a void. All three of these are known to occur in PD. Nocturia (or nocturnal enuresis) results

TABLE 1 Causes for nocturia in PD

Reduced Nocturnal Bladder Capacity	NP	Global Polyuria
• Neurogenic detrusor overactivity and/or reduced compliance • Bladder hypersensitivity (sensory urgency) • Bladder outlet obstruction (most commonly benign prostate enlargement) • Other primary urological pathologies resulting in reduced functional bladder capacity (e.g., cystitis, bladder cancer) • Incomplete bladder emptying and raised PVR	• Altered arginine vasopressin secretion • Congestive heart failure • Renal insufficiency • Excessive intake of fluid at night (especially alcohol and caffeine) • Use of long-acting diuretics • Sleep apnea	• Pituitary diabetes insipidus • Nephrogenic diabetes insipidus I • Diabetes mellitus • Psychogenic polydipsia • Electrolyte abnormality: hypercalcemia, hypokalaemia

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whenever the urine volume produced at night exceeds the functional bladder capacity. Urodynamic evidence for detrusor overactivity has been reported in 45% to 93% of PD patients[16,33,34] and correlates with scores in overactive bladder (OAB) questionnaires.[35] In urodynamic studies, 81.0% had storage disorder, 54.8% had abnormalities of storage and voiding, whereas 19.0% had only a voiding disorder.[33,36]

A likely mechanism for DO in PD is disruption of the dopamine D1-GABAergic direct pathway and its GABAergic collateral to the micturition circuit,[37,38] resulting in loss of inhibition of the micturition reflex and OAB. Severity of OAB symptoms has been shown to correlate with impairments observed on urodynamic testing and dopaminergic deficiency observed in dopamine transporter scans.[3,39]

Nocturnal Polyuria

Nocturnal polyuria (NP) is said to occur when rate of urine production is excessive only at night whereas 24-hour urine output remains within normal limits. The ICS defines NP whenever the proportion of 24-hour urine voided at night is more than 20% of the entire 24-hour urine produced in young patients and 33% in the elderly,[17,40] where the 24-hour volume is within normal limits (approximately 40 mL/kg).[17] Most published studies define NP as the proportion of 24-hour urine voided between midnight and 8 AM being more than 33%.[40] NP is under-recognized in PD. We recently reported on a group of 23 patients with PD reporting nocturia who filled in a 3-day bladder diary and standardized questionnaires assessing LUT symptoms where a surprisingly high figure of 13 patients (56.5%) were found to have nocturnal polyuria.[32] In another study, the prevalence of nocturnal polyuria was, however, found to be similar in patients with PD (at a nonsevere stage) compared to an age-matched healthy control group.[41]

There are several systems that regulate salt and water homeostasis and derangements of any of these could result in NP.[42] The renin-angiotensin-aldosterone system is the best-understood hormonal system that modulates sodium handling and ultimately promotes sodium and water reabsorption at the distal tubule. Arginine vasopressin (AVP), released from the posterior pituitary, promotes reabsorption of free water at the distal and collecting tubules.[43] Atrial natriuretic peptide (ANP) is released from the atrium of the heart and increases the glomerular filtration rate, resulting in greater excretion of sodium and water; additionally, ANP increases sodium excretion at the level of the distal convoluted tubule.

Circadian Rhythm Disturbances and Nocturia

The suprachiasmatic nucleus (SCN) of the hypothalamus controls the circadian rhythm by regulating melatonin release from the pineal gland in response to the environmental light/dark cycle.[44] Neurodegeneration and cell death occurring in PD has been shown to affect structures involved in circadian rhythm control, such as the hypothalamus. It has been shown that mice overexpressing α-synuclein exhibit a reduced SCN firing rate, potentially weakening their ability to communicate neural and hormonal signals from the central clock.[45] Sleep disturbances are common in PD,[46–48] and alterations in the circadian rhythm have been demonstrated in PD, even at the early stages.[49,50]

In health, there exists a circadian rhythm for urine production, and, as a result, roughly less than 25% of 24-hour urine is produced during the night. This is thought to be mediated through release of AVP and melatonin and is known to be affected with aging.[51] Production of urine is influenced by the circadian regulation of sodium and free water handling.[52] Diurnal release of hormones are regulated through the pituitary and increased plasma levels of arginine vasopressin at night.[51] A loss of this diurnal response has been observed in otherwise elderly healthy individuals reporting NP.[42] A loss of circadian regulation of urine production results in limited reabsorption of free water and diuresis. Reduced AVP secretion is linked not only to nocturnal polyuria,[39,53] but also to nocturnal enuresis.[53]

It is possible that circadian disturbances not only affect urine production, but also bladder functions, and a recent study using an OAB rat model demonstrated amelioration of detrusor over activity after administration of melatonin.[54]

Using melatonin[55] to treat nocturia is therefore an attractive option, and a single study has been carried out in 20 men reporting nocturia with bladder outflow obstruction attributed to benign prostate enlargement. In this randomized, double blind, placebo-controlled crossover study of controlled-release melatonin (2 mg), a significant improvement in nocturia frequency and nocturia-related bother was demonstrated after melatonin, with only minimal adverse effects.[56] This preliminary evidence seems to suggest that circadian rhythm dysregulation may contribute to nocturia; however, further studies are required to explore this possibility further.

Cardiovascular Dysautonomia and Nocturia

An association is known to exist between orthostatic hypotension (OH) and nocturia[10,57] and nocturnal polyuria.[51] In health, blood pressure (BP) is known to decrease at night, and this is often absent (nondipping of BP) in patients with PD reporting autonomic failure.[58] This may be mediated through inappropriate mineralocorticoid receptor activation.[55] Consequent to this, pressure natriuresis occurs, resulting in increased urine output and the patient reports nocturia. OH and supine hypertension frequently coexist in PD,[59] and older age, akinetic-rigid motor subtype, and pre-existing hypertension are independent risk factors for supine hypertension. Improvement of nocturia, however, has not been a consistent finding in studies evaluating treatments for supine hypertension,[55,60,61] and therefore cardiovascular dysautonomia is likely to be only one of several mechanisms responsible for nocturia in PD.

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Medical Comorbidities and Nocturia

Concomitant urological pathologies may also contribute to reduced nocturnal bladder capacity. Patients with PD may develop storage dysfunction as a result of benign prostate enlargement, which is common in the age group prevalent for PD and may cause nocturia and nocturnal polyuria.[51] Often urodynamic studies are required to evaluate the relative contribution of bladder outlet obstruction. Other urological pathologies include malignancy of the bladder, bladder stones, interstitial cystitis, and pelvic organ prolapse or from stress incontinence. Urinary tract infection can lead to urinary frequency and may exacerbate nocturia.

The treatments used to manage PD may, in themselves, influence LUT symptoms.[32] The effects of levodopa on LUT symptoms are inconsistent, however, and worsening of symptoms have been reported in some studies whereas improvement has been reported in others.[3,62,63] It has been suggested that during acute administration, L-dopa may cause worsening of symptoms, but is known to ameliorate the first sensation of bladder filling on long-term administration.[64] Dopamine receptor agonists have been reported to promote storage in a study using bromocriptine.[65] In another study, a change from bromocriptine to pergolide lessened nocturia.[46] Apomorphine was reported to increase bladder capacity.[66] DBS may have variable effects on LUT dysfunction, though an improvement in nocturia has generally been noted.[67–70]

Nocturnal Sleep Disturbances and Nocturia

Nocturnal disturbances can be observed in 70% of patients with PD and include (1) PD-related motor symptoms occurring at night; (2) PD treatment-related disturbances; (3) psychiatric symptoms; and (4) other sleep disorders, including insomnia, rapid eye movement behavioral disorder (RBD), RLS, and periodic leg movements (PLMS).[71] The urge to urinate is an important reason for awakening at night and is a potentially amenable cause for sleep disturbances in PD.[32] However, patients whose sleep is disturbed because of other reasons may void because they are awake, not necessarily because of the urge to urinate. Known as "convenience void," these voids are not therefore reflective of bladder pathology.

Nocturia is commonly reported in individuals with obstructive sleep apnea and sleep-disordered breathing.[72] This is through increased release of ANP. However, sleep apnea was not found to be a common comorbidity in patients with PD reporting nocturia in one study.[73] Considering that several of these sleep disturbances may coexist with nocturia, it is often a challenge to establish the exact contribution of these disturbances to sleep disturbance and excessive daytime sleepiness. There are no studies that have specifically evaluated this; however, the RECOVER study reported that treatment of PD patients with rotigotine improved the overall sleep quality attributed to reduced nocturnal motor symptoms (restlessness of arms or legs, urge to move arms or legs, painful posturing in the morning, and tremor on awakening), however was not associated with a reduction in episodes of nocturia[74] or improvement in urinary function.[75] The correlation between nocturia and RBD, RLS, and PD-related motor symptoms is complex and has not been specifically evaluated.

Evaluation of Nocturia in PD

History Taking and Examination[76]

Storage and voiding LUT symptoms should be enquired about during every visit. Patients may awaken at night from numerous causes and it should be explored whether this is primarily attributed to symptoms from their bladder, or a "convenience void" once they are awakened because of other reasons, such as difficulties in turning over, or RBD. Filling in a bladder diary provides a wealth of information about nocturia and is the only assessment that evaluates for nocturnal polyuria. The diary is used to record the frequency and volume of each void and provides a cost-effective prospective real-time assessment of LUT symptoms. Incorporating an urgency perception score helps to evaluate convenience voids.[77] The diary is relatively straightforward for patients to complete and provides a more accurate assessment of nighttime frequency and voided nocturnal urine volumes.[32] A recently published study highlights the importance of using bladder diaries using quantification of urine volume in the assessment of patients with PD reporting nocturia.[32] A measuring jug is needed for measuring the volume of each void by the patient and should be provided to improve accuracy.[32]

A review of the patient's current medication might reveal medications contributing to nocturia, such as long-acting diuretics. The relation between L-dopa use and LUT and motor fluctuations should be assessed. A review of past medical history would uncover other medical disorders that are known to cause nocturia, such as diabetes and heart failure. The clinical examination includes a digital rectal examination and evaluation for pelvic organ prolapse when suspected.

Investigations

Urinalysis using a reagent strips is useful to exclude a urinary tract infection, which can contribute to OAB symptoms.

Blood chemistry and urine culture (if appropriate), if not already carried out by the referring physician, form part of a basic neurourological assessment.

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Ultrasonography

The postvoid residual (PVR) urine volume is measured by ultrasound or alternatively by in-out catheterization. A raised PVR volume suggests that there is voiding dysfunction; however, it cannot be used to differentiate whether this is caused by poor detrusor contractility or by obstruction, for which urodynamics would be required.

Urodynamics

Urodynamics is useful to evaluate the cause of LUT dysfunction in PD. It helps to identify whether there is reduced bladder compliance or detrusor overactivity. It also helps to evaluate whether bladder outlet obstruction from an enlarged prostate is contributing to the problem.[76,78] There are very few urodynamic studies in PD that have looked at nocturia specifically. In one study, where nocturia was reported in 77.5% patients with PD, the urodynamic tests revealed neurogenic detrusor overactivity in 33 patients (67.3%), detrusor underactivity in 6 (12.2%), and 10 (20.4%) with normal detrusor function.[12]

Uchiyama et al.[36] found nocturia in 38.0% of the 50 patients assessed using a nonvalidated questionnaire. Most of the patients had abnormalities in urodynamic studies.[36] These studies suggest detrusor overactivity to be more common in urodynamic studies in PD with nocturia.

Other Urological Investigations

In cases of obstructive features, urethrocystoscopy (combined with bladder washing cytology, if appropriate) might be needed. Table 2 summarizes the clinical assessment of nocturia in PD.[76]

Strategies for Managing Nocturia in PD

Despite the high prevalence of nocturia and impact on QoL, treatment options for managing this problem are currently limited and are often poorly tolerated or ineffective in PD. Guidance on nocturia treatment is limited, and most treatment options are derived from guidance around general management of urinary symptoms in neurological patients.[57,76,79]

Conservative Measures

Studies specifically evaluating nocturia management in PD using conservative measures are lacking. There is evidence, however, in the urology literature showing that simple lifestyle interventions and behavioral modifications can help nocturia, and it is reasonable to suggest these options be tried in PD patients reporting nocturia. These include reducing fluid intake,[80] caffeine, and/or alcohol and large meals a few hours before going to bed. In those with dependent edema, advice may be given promoting exercise, elevating the legs in the afternoon to a level above the heart, and use of compression stockings. Patients are encouraged to empty the bladder before going to bed. Diuretics given during the late afternoon or early evening may also help to reduce third-space fluid. If given later during the evening, however, diuretics may increase nocturia.[81] If conservative treatment fails to control the patient's symptoms, then medical treatment is aimed at the primary cause of the nocturia. Incomplete bladder emptying is unusual in PD-related LUT dysfunction; however, if high PVR volume is associated with nocturia in PD, catheterization before going to bed improves the functional bladder capacity and thereby help with nocturia. In patients with PD and nocturia to avoid falls and other complications, the path to the toilet should be lit and the area should be made "falls safe" to avoid falls and injuries. In patients with limited mobility, but preserved continence, simple measures such as a bedside commode or flask can eliminate the use of pads or catheter in these patients.

PD-Specific Treatment

Dopaminergic Treatment

There are not many studies with dopamine or dopamine agonists specifically in nocturia. In an open-label study including 3 patients, 12 weeks of treatment with pergolide improved nocturia frequency in all 3 patients and an improvement of sleep QoL in 2.[63]

DBS

DBS is a well-accepted treatment option in advanced PD. Although the studies have not specifically focused on nocturia,

TABLE 2 Clinical assessment of nocturia in PD (modified from Panicker et al.[69])

	Bedside Evaluation	Noninvasive Tests	Invasive Tests (Only If Needed)
Essential	History taking; physical examination; bladder diary	Urinalysis; PVR urine volume measurement; ultrasonography	
Desirable	Questionnaires	Uroflowmetry; blood biochemistry	
Required in specific situations		Urine culture; urine cytology	(Video-)urodynamics with pressure-flow studies; urethrocystoscopy; pelvic neurophysiology; renal scintigraphy

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there is evidence that STN-DBS-treated patients exhibit significantly less nocturia. In a study comparing DBS (globus pallidus interna) and other forms of treatment in 107 patients with PD, the overall amount of urinary symptoms were similar, but fewer DBS patients (47%) complained of nocturia, compared to conventionally treated (88%), and to apomorphine pump-treated (66%), patients.[82] Not only did the patients who had DBS report less nocturia ($P = 0.007$), they were also less bothered by nocturia ($P = 0.01$), compared to the other treatment groups, as assessed by Danish Prostate Symptom Score.[82] More studies may be needed to establish definite correlation and to understand the pathophysiology of this association.

Management Specifically for LUT Symptoms

Management of Reduced Functional Bladder Capacity

Antimuscarinic Agents

Antimuscarinic medications are the first-line treatment for bladder storage symptoms and detrusor overactivity.[83] Oxybutynin, tolterodine, solifenacin, and trospium chloride have beneficial effects on nocturia.[40] If prescribed, a low dose is initially recommended with a progressive increasing dosage. Furthermore, the strict respect of the scheduled taking is important in order to reduce nonurinary anticholinergic effects.

However, their side-effect profile, which corresponds to an increasing anticholinergic burden, limits their use. The risk of urinary retention has not been specifically assessed in PD. Consequently, a repeated PVR measurement is recommended. In addition, constipation was reported not to be increased in parkinsonian patients using antimuscarinics.[84] Of particular concern is the impact on cognitive functions in patients with PD, especially in the elderly. Anticholinergic medications can add to the anticholinergic burden of antiparkinsonian therapy and thus to the cognitive dysfunction (e.g., mild cognitive impairment or dementia).[76] Drugs such as trospium chloride or tolterodine, which do not cross the blood–brain barrier, have may be preferred.[85] However, evidence supporting these considerations in clinical practice is limited,[86] and caution is advised when using an antimuscarinic agent in PD.

A recent a double-blind, randomized, placebo-controlled study evaluated solifenacin in 23 patients with PD and urinary symptoms. There was no significant improvement during the double-blind phase, but in the open-label extension phase, there was an improvement in the number of micturition per 24-hour period at a mean dose of 6 mg/day ($P = 0.01$) and the number of nocturia episodes per 24-hour period ($P = 0.01$).[87] The drug was well tolerated, and solifenacin did not cause any cognitive side effects. Reported side effects included constipation (n = 1) and xerostomia (n = 2) and urinary retention (n = 1). Though reduction in nocturia was reported in the open label phase, it is difficult to draw definite conclusions from this study on the efficacy of solifenacin in nocturia.

Botulinum Toxin

Detrusor injection of botulinum toxin has been proven useful in neurogenic bladder attributed to spinal cord disease[88] or multiple sclerosis[89]; however, the likelihood of incomplete bladder emptying or urinary retention and the need to use a catheter is a limiting factor.[90,91] Little is known about its value in patients with PD.

All studies included a limited number of patients (respectively 6,[90] 8,[92] and 16 patients[91]) with short follow-up (5,[90] 6,[92] and 12 months[91]) and used small doses of botulinum toxin (200 U)[90] (100 U[92]; BoNTA Dysport) and 500 U.[91] In all three studies, the use of a low dose of toxin A was effective on overactive bladder (improving bladder capacity, reduction in frequency of urinary leakage and urination, and improving bladder capacity) and improving QoL.[90]

Giannantoni et al. reported, in 2009,[90] an increased PVR in all patients with the need to perform to self-intermittent catheterization in 1 patient. The same investigators reported, in 2011,[92] an increased PVR in 2 patients with both the need to perform self-intermittent catheterization.

Finally, Kulacksizoglu et al.[91] have reported no increase in PVR. Risk of retention has to be carefully evaluated given the potential difficulty to perform self-intermittent catheterization for patients with PD. Use of botulinum injections in PD may be based on recommendations in other conditions with neurogenic bladder.[90,93]

Neuromodulation

Sacral nerve modulation and percutaneous tibial nerve stimulation (PTNS) are other options that can be tried in refractory cases of storage symptoms in case of failure, intolerance, or contraindications to medical treatment. There is insufficient data of their efficacy in PD or MSA.[94,95] Acute PTNS has been reported to increase functional bladder capacity in PD.[96] In addition, chronic stimulation has been reported to decrease frequency, as well as urinary and urge urinary incontinence. However, long-term outcomes in PD are lacking.[96]

No studies have specifically evaluated the outcomes of sacral neuromodulation in PD. The existing studies only included a limited number of p-arkinsonian patients and were retrospective. In a retrospective study, Wallace et al. reported a decrease of nocturia of 70% in 33 neurological patients, among whom 4 had PD.[95]

Management of Incomplete Bladder Emptying

Incomplete bladder emptying is less common in PD, but may be observed. If identified, medications used for prostate enlargement may be tried specifically in middle-aged males.

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TABLE 3 Management of nocturia in PD

Management of the OAB	Management of Incomplete Bladder Emptying	Management of NP
• Antimuscarinic agents • Tibial neuromodulation • Detrusor onabotulinumtoxinA injections	• α-adrenoceptor blockers • Intermittent catheterization	• Desmopressin • Late-afternoon diuretic

Intermittent self-catheterization have become the mainstay of treatment of disorders associated with incomplete bladder emptying, but there are specific issues related to dexterity in PD, which may make this challenging.[97]

Management of NP

There are only limited options for managing NP. Desmopressin has been tried[98–100] in parkinsonian syndrome, including PD and MSA, but long-term follow-up is lacking. Because hyponatremia is common, caution is advised in people over 65 years of age, limiting its use in PD. However, the risk of hyponatremia increases with advancing age and the British National Formulary advises caution when this is used in individuals over the age of 65. Using a diuretic in the late afternoon is an alternative,[101] and though this has not been studied specifically in people with PD, possible exacerbation of hypotension in those with concomitant postural hypotension is a concern.[11] Table 3 summarizes the management of nocturia.

Management of Circadian Dysregulation

The nighttime awakenings associated with motor complications and RBDs or other nocturnal disturbances in PD may contribute to convenience voids. So far, there is no study addressing the nature of nocturnal awakenings and their association with nocturia. In this regard melatonin may be a useful strategy in managing nocturia and NP in PD. A single-center, open-label exploratory phase IIb pilot study incorporating sleep accelerometer and sleep diary is ongoing with the main objective to evaluate melatonin for the treatment of nocturia in adults with PD.[102] Further studies are needed regarding management of sleep disturbances, motor complications, and to know whether these strategies may also help manage nocturia related to convenience voids.

Conclusion

Nocturia is one of the commonest NMS in PD, which significantly impacts QoL in patients with PD. Nocturia is a symptom that manifests as a result of an underlying cause, such as reduced bladder capacity, NP, or circadian dysregulation. There are several therapeutic strategies, and an individualized approach is recommended to optimize the management of nocturia.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

A.B.: 1B, 1C, 3A, 3B
V.P.: 1C, 3B
L.D.: 1C, 3B
J.N.P.: 1A, 2A, 3A, 3B

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